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Editorial

Let This Be Our New Year's Pledge

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2016 was a remarkable year, a year of significant advances in cancer biology and treatment, a year of social and political transition, and a year of sadness for those of us who have lost dear friends in the field of cancer research. Please join us as we share some reflections on these events.

Cancer immunotherapy clearly occupies center stage in treatment research. At the clinical end, we have watched the steady advancement of checkpoint therapy into valuable use in many solid tumors with 15%–20% response rates, many of which are durable, now the norm for tumors of the respiratory, genitourinary, and gastrointestinal tracts, and even greater benefit is realized for melanoma [1] and Merkel cell tumors [2, 3]. At the same time, we recognize the enormous costs of these new drugs and our inability at present to select the right patients for treatment [4]. PDL-1 expression and mutational burden seem to allow for enrichment of response for lung cancer patients but are imperfect biomarkers, as these drugs occasionally benefit low expressing tumors. We hope that better biomarkers for clinical response and patient benefit will soon be forthcoming.

The U.S. Food and Drug Administration (FDA) continues to lend strong support to the rapid advancement of new compounds to patient benefit. A number of novel and effective small molecules were approved in 2016, notably venetoclax, a Bcl-2 inhibitor for chronic lymphocytic leukemia (CLL) [5]; palbociclib, a CDK 4/6 inhibitor, for estrogen receptor positive breast cancer [6]; rucaparib, a potent PARP inhibitor, for ovarian cancer [7]; and cabozantinib, a c-MET and VEGFR inhibitor, for first-line treatment of renal cancers [8]. Each of these therapies builds upon fundamental research supported by the National Institutes of Health (NIH) and, in particular, the National Cancer Institute (NCI). A host of new monoclonal antibodies were also approved, advancing treatment of multiple myeloma, CLL, and solid tumors [9]. The FDA's Office of Hematology and Oncology Products (OHOP) and its Oncology Center of Excellence deserve great praise for their swift action on many worthwhile agents.

Appropriately, cancer research has been very much in the public eye in 2016, thanks to the efforts of Vice President Joe Biden in promoting a national dialogue on cancer. In one of the few congressional actions that reflected bipartisan cooperation, the 21st Century Cures Act passed both the House and Senate following the presidential election, and authorized a major increase of $1.8 billion to fund cancer research over a number of years. The U.S. Senate renamed the research portion of the Cancer Moonshot Task Force the "Beau Biden Cancer Moonshot" in honor of the vice president's late son, who died of a glioma in 2015 at age 46. The bill also aims to strengthen addiction research and mental health services, and authorizes additional funds for both the NIH and FDA. We are cautiously hopeful that these authorizations will lead to significant multiyear appropriation of funds for cancer research.

We also note with an air of expectation, the emerging importance of "big data" in the strategy outlined in Biden's Cancer Moonshot initiative. Transparency through data sharing, data curation, and data aggregation enable multiple users to undertake analyses that offer new insights and important discoveries that are just beginning to be published [10, 11]. We are particularly proud of the rapidly expanding open source data base, Project Data Sphere®, which consists of ~41,000 subjects of industry and government supported trials. This growing resource is now freely available for researchers' use online. Proof of principle has already been achieved using this initiative of the nonprofit CEO Roundtable on Cancer [12].

We would be remiss if we did not address the implications of the U.S. presidential and congressional election of 2016. These results have injected a high degree of uncertainty about issues that directly impact cancer research and

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treatment. Will the leadership of the NIH and the NCI change in President Trump's new administration? Will the new leadership be sympathetic to the cause of cancer research? The nominee for Secretary of Health and Human Service (HHS), Tom Price, an orthopedist and congressman from Georgia, seems focused on replacing "Obamacare" (i.e., Affordable Care Act) and as a member of the House Tea Party Caucus lambasted the "vile liberal agenda" [13]. Will supporting science in next year's HHS take a back seat to cutting programs and entitlements?

Although the future leadership of the FDA also awaits the new President's appointment and the U.S. Senate's confirmation, we hope that President-elect Trump's transition team looks carefully at both the credentials and leadership of the current Commissioner Rob Califf who has both the vision and demonstrated capacity to guide this vital federal regulatory agency, in keeping with the FDA's mission, toward innovative research, not just food and drug regulation.

There are two other important issues in play. First, high drug prices, especially for cancer drugs, have become a subject of serious concern for both Democrats and Republicans, as well as for our patients, and for our profession. The President-elect has called for negotiation of drug prices for drugs purchased through Medicare, a startling departure for a Republican administration. It is uncertain whether substantial efforts to control prices of drugs will result, but never before has the issue commanded such front page press and broad interest.

A second matter of some concern is the possibility that criteria for FDA drug approval may be in flux. One prominent and possible candidate for FDA Commissioner has expressed the opinion that safety should be the lone criterion for drug approval and that efficacy should be left to the opinion/decision of the prescribing physician [14]. This position represents a radical departure from important reforms of the last century, reforms that have emphasized the importance of proving efficacy as a predicate for FDA drug approval. We believe that the medical research community should strongly oppose this stance. The safety of snake oil and shark cartilage should not qualify them as approvable drugs, simply because they don't inflict serious bodily harm. The public would waste precious time, money, and the opportunity for real drug benefit if the sale of ineffective medicines is allowed by the FDA.

As we begin our New Year of 2017, we quietly pause with great sadness as we also reflect on the loss of treasured colleagues and precious friends, Eddie Reed in 2015 [15], and Gregory Curt in 2016 [16, 17], who succumbed to the disease, and Dan Sargent who suffered fatal late side effects of cancer treatment [18]. We cannot give up the fight against cancer until, like ISIS, it is no longer the terrorist in our midst that threatens us all. Let us be mindful that the patient losses due to cancer vastly outnumber the deaths in all the wars and revolutions of the current decade.

Cancer not only deserves our attention, it demands a lasting and forceful commitment by both the government and from each of us as private citizens. That is the only fitting memorial to those whose lives have been foreshortened.

Let this be our New Year's pledge: *not to give in or give up . . . ever*!

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